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Reply to the Editor:

We thank Pocar and colleagues for their interest in our article regarding surgery for acute type A aortic dissection in the setting of stroke.[1] We also acknowledge their recent report about repairing acute type A aortic dissection in patients with coma.[2] As was pointed out in their report, the use of the Glasgow Coma Scale (GCS) to exclude patients for type A aortic repair was not relevant. Specifically, they noted that all 5 of their patients would have been considered severely brain injured (GCS $<$ 8) based on the GCS alone. We do appreciate and concur with this point and also congratulate them for them for their results in this very difficult subgroup of patients.

Although the GCS, the National Institutes of Health Stroke Scale (NIHSS), and Rankin score for that matter may not be completely applicable in the setting of acute type A aortic dissection, we wanted to analyze these patients with objective criteria. We do believe that the NIHSS and the Rankin score may be helpful, although this study was not powered to demonstrate this. Because we recommended that operative repair was indicated in patients *without* "neurologic devastation" or coma, we attempted to provide some objective criteria for this condition, hence the use of these scales and scores. Regarding the 1 nonoperated patient who was considered neurologically devastated, we acknowledge that one cannot derive any conclusions in relation to defining neurologic devastation. In fact, it was the appearance of the patient's computed tomography scan of the head, which showed bilateral massive infarction, that ultimately led to his nonoperative course.

Prior to the results of this study, we maintained that stroke was a relative contraindication to immediate repair for acute type A aortic dissection. We have since modified our approach and have become more aggressive in repairing acute type A aortic dissection in patients with stroke. Our experience in patients with coma, however, has been limited and thus we continue to maintain a selective approach in patients with coma and neurologic devastation. We admit that GCS is not a good measure of coma or neurologic devastation, and radiographic evaluation, in the hemodynamically stable patient, may be more helpful. How coma and neurologic devastation are determined and whether or not surgery is performed, however, should be left ultimately to the neurologist and operating surgeon, respectively.

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High-dose atorvastatin is associated with impaired myocardial angiogenesis in response to vascular endothelial growth factor in hypercholesterolemic swine: Relevance to the human situation?

To the Editor:

We read with great interest the article by Boodhwani and colleagues[1] regarding the impact of high-dose statin therapy on vascular endothelial growth factor-A (VEGF-A)–induced myocardial angiogenesis in a hypercholesterolemic pig model of chronic ischemia. This article demonstrated that collateral-dependent myocardial perfusion remained impaired in hypercholesterolemic and atorvastatin-treated pigs in response to additional treatment with VEGF-A relative to a normocholesterolemic control group. It concluded that a high-dose statin therapy was not associated with improved myocardial neovascularization. In that study, however, the hypercholesterolemic pigs were treated with an atorvastatin dosage of 3 mg/(kg · d), which exceeds the maximal possible dosage in patients (80 mg/d) by a factor of about 3.

To achieve at least moderate cholesterol lowering, pigs need to be treated with high-dose statins because of lesser lipid-lowering potency and efficacy in pigs relative to human beings.[2] One must remain aware, however, of the increased risk of adverse events with extremely high statin dosages. In their article, Boodhwani and colleagues[1] described a clearly decreased capillary endothelial cell density in the ischemic territory in the hypercholesterolemic and atorvastatin-treated pigs relative to the normocholesterolemic pigs and even the untreated hypercholesterolemic animals. To exclude the possibility that the hypercholesterolemic and atorvastatin-treated pigs suffered potential toxic (cellular) side effects of atorvastatin that might explain the neovascularization impairment, the investigators should have incorporated a control group of normocholesterolemic pigs treated with the same atorvastatin dosage. Moreover, treatment of the hypercholesterolemic pigs with lower atorvastatin dosages, more relevant to the human situation, might demonstrate whether there are potential dose-dependent toxic cellular side effects. Indeed, a recently published article by Chade and associates[3] indicates that statins used in an intermediate (human) dosage in pigs do lead to a stimulation of arteriogenesis. Furthermore, a retrospective clinical study supports the view that intensified statin treatment is associated with an improved arteriogenic response in human beings.[4]

Another piece of evidence for statin overdose in the hypercholesterolemic pigs of Boodhwani and colleagues[1] might be the observation of prolonged *Akt* activation in the atorvastatin-treated pigs. Therefore, the *Akt* downstream signal transduction pathways in endothelial cells might not any longer be able to respond adequately to other pathophysiologic stimuli. Indeed, it has been demonstrated that a prolonged *Akt* activation is associated with detrimental cardiac effects in an ischemic mouse model,[5] as was even cited by Boodhwani and colleagues[1] in their article.

Taken together, we believe that it is not appropriate to compare directly the arteriogenic effects of high-dose statin treatment in pigs and human beings in light of the approximately 3-fold higher statin dosage used in pigs.